Impact of vitamins & nutrients on neurological function

Vitamin E and D

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Lecture Outline

• Topics from last week
  • How do we hear?
  • Disrupting a neural network
  • Choline measurement in blood
  • Recommendations for vitamin and nutrient intake
  • Blood Brain Barrier
  • The Institute of Holistic Nutrition

• Vitamin E
• Vitamin D
How do we hear?

1. Sound waves enter your outer ear and travel through the ear canal to your eardrum.

2. Your eardrum vibrates with the incoming sound and sends the vibrations to three tiny bones in your middle ear.

3. The bones in your middle ear amplify the sound vibrations and send them to your inner ear, or cochlea. The sound vibrations activate tiny hair cells in the inner ear, which in turn release neurochemical messengers.

4. Your auditory nerve carries this electrical signal to the brain, which translates it into a sound you can understand.
How do we hear?

https://www.youtube.com/watch?v=2U57tFpOLYI
How to disrupt a message

-neuron dies in the neural network
-drugs/toxins/brain damage/brain disease
-neural network not stimulated
How is choline measured in blood?

- Choline (free and total), 7 to 20 μM, average 10 μM
- Betaine
Recommendations for intake of vitamins and nutrients

Health Canada

Transportation into Blood Brain Barrier

- Passive Diffusion

- Active Diffusion
Blood Brain Barrier

**diffusion (simple)**
- small molecules: H₂O, O₂, CO₂, Na⁺, Ethanol
- lipophilic substances: steroid hormones

**special transport proteins**
- glucose: GLUT-1
- amino acids

**transcytosis**
- transporters

**blood**

**brain**
Vitamin E

• Found naturally in vegetables (green vegetables), nuts and nut oils, dairy products, meat and fish

• Gamma-tocopherol, most common form found in North American diet

• Alpha-tocopherol biological active form of vitamin E, second most common form of Vitamin E in diet

• Association with vitamin E levels and cardiovascular disease
Vitamin E

• Plays a role as an antioxidant

• **Antioxidants** are man-made or natural substances that may prevent or delay some types of cell damage.

• **Antioxidants** are found in many foods, including fruits and vegetables. They are also available as dietary supplements.
Free Radicals

Free Radical is an uncharged molecule (typically highly reactive and short-lived) having an unpaired valence electron.

[Diagram showing a free radical and its impact on other molecules, labeled as "Defenseless and Damaged."]

http://dhealthybites.com
Free Radicals
Antioxidants

Antioxidants Doing their Job

Healthy Cell Membrane

Antioxidant neutralizing a free radical

HUMAN CELL

Damaging Free Radicals

NUCLEUS

Free radical missing an electron in its outer shell

Antioxidants have extra electrons that they can donate to free radicals
Vitamin E Recommended intake

<table>
<thead>
<tr>
<th>mg/day</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>0 to 6 months</td>
</tr>
<tr>
<td>5</td>
<td>7 to 12 months</td>
</tr>
<tr>
<td></td>
<td><strong>Children</strong></td>
</tr>
<tr>
<td>6</td>
<td>1 to 3 years</td>
</tr>
<tr>
<td>7</td>
<td>4 to 8 years</td>
</tr>
<tr>
<td>11</td>
<td>9 to 13 years</td>
</tr>
<tr>
<td></td>
<td><strong>Adolescents and adults</strong></td>
</tr>
<tr>
<td>15</td>
<td>14 and older</td>
</tr>
</tbody>
</table>
Vitamin E and neurological function

• The role of vitamin E and brain is not very clear

• Study in rats found….
  • Deprived of alpha-tocopherol over one year
  • Loss of alpha-tocopherol less rapid in neural tissue (e.g. brain, spinal cord and nerves) than in non-neural tissue (e.g. liver, blood)
  • Neural tissues conserve vitamin E
Vitamin E and neurological function

• Lipid peroxidation increased in brain as a result of vitamin E deficiency
• Lipid peroxidation is the oxidative degradation of lipids (fat)
Vitamin E and neurological function

Normal membrane

Lipid peroxidation

- Integral protein
- Peripheral protein
Questions?
Break
Vitamin E and Alzheimer's disease

• Oxidative stress is involved in pathogenesis of Alzheimer’s disease
• Brain contains high levels of oxidable lipids (fats vulnerable to oxidative stress)
• 2004 studies suggest that Vitamin E might be effective at reducing levels of oxidative stress in AD patients
Placebo

• Placebo: is a substance or treatment with no active therapeutic effect

• Medical Research: placebo can be made to resemble an active medication or therapy so that it function as control

• Placebo effect: recipient perceives an improvement in condition due to personal expectation
Vitamin E and Alzheimer's disease

- No treatment that will delay, prevent or cure Alzheimer’s disease (AD)
- Current therapies: slow functional decline
- Study in 2014
- Made headlines: Vitamin E can cure AD
Vitamin E and Alzheimer's disease

• 613 patients aged 53 to 96 with diagnosis of possible or probable AD
• Memantine: glutamatergic drug
• Treatments:
  • Vitamin E + Memantine Placebo
  • Memantine + vitamin E placebo
  • Both vitamin E and Memantine
  • Two placebos
Vitamin E and Alzheimer's disease

• Outcome measure was a AD questionnaire
  • Functional abilities to perform activities of daily living
• All participants got worse over the period of the study
• Subjects in vitamin E group had significantly slower decline
• Group taking both vitamin E and memantine did significantly worse than the group taking vitamin E along
Vitamin E and Dementia

• Review published in 2017, summarized a number of studies
• GOAL: Effectiveness for vitamin E in treating people with Alzheimer’s disease or mild cognitive impairment (MCI)
Vitamin E and Dementia

• Vitamin E did not reduce the number of people with MCI who developed dementia over 3 years

• Vitamin E did not improve cognition (e.g. learning or memory) in people with dementia due to AD
Vitamin E and Dementia

• One study found that people with dementia due to AD who took vitamin E could manage daily activities (e.g. bathing, dressing) better than people who took placebo

• FINDINGS: No benefits or harms from vitamin E supplements

• Different types or doses of vitamin E might have different effects
Vitamin E and stroke

- Supplementation with vitamin E
  - Increases risk of haemorrhagic stroke by 22%
  - Decreases risk of ischaemic stroke by 10%

- More information: http://www.bmj.com/content/341/bmj.c5702.full
Vitamin E Summary Video
https://www.youtube.com/watch?v=N8ZJIEMQ2Qg
Vitamin D Metabolism

• Obtained from diet (e.g. dairy or fish) or environment (e.g. sun)
• Converted to active form in liver in order to participate in physiological function, for example:
  • Inhibition of growth of cancer cells
  • Protection against immune diseases
Vitamin D Recommended Intake

<table>
<thead>
<tr>
<th>Age group</th>
<th>RDA (IU/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants 0–6 months</td>
<td>400*</td>
</tr>
<tr>
<td>Infants 6–12 months</td>
<td>400*</td>
</tr>
<tr>
<td>1–70 years</td>
<td>600 (15 µg/day)</td>
</tr>
<tr>
<td>71+ years</td>
<td>800 (20 µg/day)</td>
</tr>
<tr>
<td>Pregnant/Lactating</td>
<td>600 (15 µg/day)</td>
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</tbody>
</table>
Vitamin D and Neurological Function

• Development of brain (neurogenesis)
• Neurotransmission (neurotransmitters: acetylcholine, dopamine, serotonin)
• Neuroprotection
  • after ischemia (stroke)
  • Parkinson’s disease (anti-neurodegenerative)
Vitamin D and Neurological Function

• Neuroimmunodulation
  • Microglial cells
    • Type of glial cells
    • Immune cells in the brain
    • 10-15% of cells in the brain
Vitamin D and Neurological Function

- Neuroimmunodulation
  - Microglial cells
Vitamin D and Neurological Function

- Neurotrophic factors
  - Growth factors in the brain help neurons develop or maintenance of mature neurons
- Vitamin D involved in synthesis of:
  - Growth derived neurotrophic factor: GDNF
  - Neurotrophin-3: NT-3
Vitamin D and Neurological Function

- Neurotrophic factors

Nerve Growth Factors (shown in green) is required by neurons in order to survive. As they are a limited extracellular resource, some neurons (shown in blue) may uptake a disproportionate share of survival factors, leading to the eventual death of neighboring neurons (shown in red).
Vitamin D and Neurological Function

- Deficiency of Vitamin D associated with neurological and psychiatric disorders
- Hypovitaminosis D (too little vitamin D) associated with neuromuscular disorders, dementia and Parkinson’s disease
Causes of Alzheimer's disease

- Hyperhomocysteinemia
- Diabetes
- Metal stress
- Head injury
- Vitamin D deficiency
- Psychological stress
- Folate, B12 deficiency
- Vascular injury

Secondary trigger

Environmental and metabolic risk factors

Genetic/epigenetic modulation

Mechanisms

- Oxidative stress
- Calcium imbalance
- Disturbed neurotrophin and NT homeostasis
- Neuronal hypometabolism
- Abnormal protein accumulation
- Mitochondrial dysfunction

Neuronal degeneration and neuronal death

Aging

Inflammation

Sedentary lifestyle
Vitamin D and Alzheimer's disease

• Low levels of vitamin D have been linked to cognitive decline
• Trial of vitamin D alone or in combination with other agents/anti-AD drugs have shown positive results in some recent works
• Combined use of vitamin D₃ and DHA (Docosahexaenoic acid) is an emerging novel strategy to enhance direct and immune protection of neurons against brain amyloidosis and other brain insults
• Cognition nor disability changed significantly after high-dose vitamin D in mild to moderately severe AD cases
Vitamin D and Alzheimer's disease

• arguments against vitamin D supplementation are based on the small number of clinical trials
• randomized clinical trials (RCTs) to test the effectiveness of vitamin D supplements against placebo in patients with AD are essentially needed at this time
Vitamin D and Alzheimer's disease

www.youtube.com/watch?v=Fr8hjVS2x5c
Multiple Sclerosis

- demyelinating disease
- environmental risk factors
- autoimmune
MULTIPLE SCLEROSIS

Healthy

Nerve affected by MS

Schwann cells
Node of Ranvier
Nerve fiber

Damaged myelin
Exposed fiber
Multiple Sclerosis & Vitamin D

- Vitamin D deficiency a risk factor for multiple sclerosis
- Vitamin D plays a role in regulation, proliferation, differentiation and immunomodulation in central nervous system
Basic Science and Multiple Sclerosis

- In laboratory animals....
- Vitamin D deficiency responsible for worsening of symptoms
- Supplementation with vitamin D made symptoms disappear

- Human Data not clear
Recent human study from McGill University.....

• Investigated the link between Vitamin D metabolism and risk of Multiple Sclerosis development

• European population
• Single nucleotide polymorphisms (SNPs) of enzymes involved in Vitamin D metabolism

Mokry et al., 2015
Single nucleotide polymorphism (SNPs)

is a variation in a **single nucleotide** which may occur at some specific position in the genome (DNA).
Study investigated genetic changes in enzymes involved in vitamin D metabolism.
Findings……

- Genetically lowered levels of 25OHD associated with increased risk of Multiple Sclerosis in European population
Multiple Sclerosis, Vitamin D and Fatigue

https://www.youtube.com/watch?v=LFL4jDPIXsk
Vitamin D and K1

• Vitamin K works with vitamin D to regulate:
  • Bone resorption
  • Activation
  • Distribution

• Muscle regeneration (Vitamin D (i.e. dosages up to 4000-5000 IU/day), in combination with 50 to 1000 mcg/day of vitamin K₁ and K₂)
  • increase skeletal muscle function
  • decrease recovery time from training
  • increase both force and power production
  • increase testosterone production, each of which could potentiate athletic performance

More information: http://pubmedcentralcanada.ca/pmcc/articles/PMC4539891/
Questions?

Next week….Over Supplementation